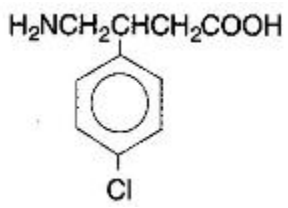
LIORESAL - baclofen tablet
Novartis Pharmaceuticals Corporation

C98-22 (Rev. 4/98)
667794

Lioresal®
baclofen USP
Tablets
10 mg
20 mg
Muscle Relaxant, Antispastic
Rx only
Prescribing Information

DESCRIPTION

Lioresal, baclofen USP, is a muscle relaxant and antispastic, available as 10-mg and 20-mg tablets for oral administration. Its chemical name is 4-amino-3-(4-chlorophenyl)- butanoic acid, and its structural formula is



Baclofen USP is a white to off-white, odorless or practically odorless crystalline powder, with a molecular weight of 213.66. It is slightly soluble in water, very slightly soluble in methanol, and insoluble in chloroform.
Inactive Ingredients. Cellulose compounds, magnesium stearate, povidone, and starch.

ACTIONS

The precise mechanism of action of Lioresal is not fully known. Lioresal is capable of inhibiting both monosynaptic and polysynaptic reflexes at the spinal level, possibly by hyperpolarization of afferent terminals, although actions at supraspinal sites may also occur and contribute to its clinical effect. Although Lioresal is an analog of the putative inhibitory neurotransmitter gamma-aminobutyric acid (GABA), there is no conclusive evidence that actions on GABA systems are involved in the production of its clinical effects. In studies with animals, Lioresal has been shown to have general CNS depressant properties as indicated by the production of sedation with tolerance, somnolence, ataxia, and respiratory and cardiovascular depression. Lioresal is rapidly and extensively absorbed and eliminated. Absorption may be dose-dependent, being reduced with increasing doses. Lioresal is excreted primarily by the kidney in unchanged form and there is relatively large intersubject variation in absorption and/or elimination.

INDICATIONS

Lioresal is useful for the alleviation of signs and symptoms of spasticity resulting from multiple sclerosis, particularly for the relief of flexor spasms and concomitant pain, clonus, and muscular rigidity.
Patients should have reversible spasticity so that Lioresal treatment will aid in restoring residual function.
Lioresal may also be of some value in patients with spinal cord injuries and other spinal cord diseases.
Lioresal is not indicated in the treatment of skeletal muscle spasm resulting from rheumatic disorders.
The efficacy of Lioresal in stroke, cerebral palsy, and Parkinson's disease has not been established and, therefore, it is not recommended for these conditions.

CONTRAINDICATIONS

Hypersensitivity to baclofen.

WARNINGS

a. Abrupt Drug Withdrawal:

Hallucinations and seizures have occurred on abrupt withdrawal of Lioresal. Therefore, except for serious adverse reactions, the dose should be reduced slowly when the drug is discontinued.

b. Impaired Renal Function:

Because Lioresal is primarily excreted unchanged through the kidneys, it should be given with caution, and it may be necessary to reduce the dosage.

c. Stroke:
Lioresal has not significantly benefited patients with stroke. These patients have also shown poor tolerability to the drug.

d. Pregnancy:
Lioresal has been shown to increase the incidence of omphaloceles (ventral hernias) in fetuses of rats given approximately 13 times the maximum dose recommended for human use, at a dose which caused significant reductions in food intake and weight gain in dams. This abnormality was not seen in mice or rabbits. There was also an increased incidence of incomplete sternebral ossification in fetuses of rats given approximately 13 times the maximum recommended human dose, and an increased incidence of unossified phalangeal nuclei of forelimbs and hindlimbs in fetuses of rabbits given approximately 7 times the maximum recommended human dose. In mice, no teratogenic effects were observed, although reductions in mean fetal weight with consequent delays in skeletal ossification were present when dams were given 17 or 34 times the human daily dose. There are no studies in pregnant women. Lioresal should be used during pregnancy only if the benefit clearly justifies the potential risk to the fetus.

PRECAUTIONS
Because of the possibility of sedation, patients should be cautioned regarding the operation of automobiles or other dangerous machinery, and activities made hazardous by decreased alertness. Patients should also be cautioned that the central nervous system effects of Lioresal may be additive to those of alcohol and other CNS depressants.
Lioresal should be used with caution where spasticity is utilized to sustain upright posture and balance in locomotion or whenever spasticity is utilized to obtain increased function.
In patients with epilepsy, the clinical state and electroencephalogram should be monitored at regular intervals, since deterioration in seizure control and EEG have been reported occasionally in patients taking Lioresal.
It is not known whether this drug is excreted in human milk. As a general rule, nursing should not be undertaken while a patient is on a drug since many drugs are excreted in human milk.
A dose-related increase in incidence of ovarian cysts and a less marked increase in enlarged and/or hemorrhagic adrenal glands was observed in female rats treated chronically with Lioresal.
Ovarian cysts have been found by palpation in about 4% of the multiple sclerosis patients that were treated with Lioresal for up to one year. In most cases these cysts disappeared spontaneously while patients continued to receive the drug. Ovarian cysts are estimated to occur spontaneously in approximately 1% to 5% of the normal female population.

PEDIATRIC USE
Safety and effectiveness in pediatric patients below the age of 12 years have not been established.

ADVERSE REACTIONS
The most common is transient drowsiness (10%-63%). In one controlled study of 175 patients, transient drowsiness was observed in 63% of those receiving Lioresal compared to 36% of those in the placebo group. Other common adverse reactions are dizziness (5%-15%), weakness (5%-15%) and fatigue (2%-4%). Others reported:

Neuropsychiatric:
Confusion (1%-11%), headache (4%-8%), insomnia (2%-7%); and, rarely, euphoria, excitement, depression, hallucinations, paresthesia, muscle pain, tinnitus, slurred speech, coordination disorder, tremor, rigidity, dystonia, ataxia, blurred vision, nystagmus, strabismus, miosis, mydriasis, diplopia, dysarthria, epileptic seizure.

Cardiovascular:
Hypotension (0%-9%). Rare instances of dyspnea, palpitation, chest pain, syncope.

Gastrointestinal:
Nausea (4%-12%), constipation (2%-6%); and, rarely, dry mouth, anorexia, taste disorder, abdominal pain, vomiting, diarrhea, and positive test for occult blood in stool.

Genitourinary:
Urinary frequency (2%-6%); and, rarely, enuresis, urinary retention, dysuria, impotence, inability to ejaculate, nocturia, hematuria.

Other:
Instances of rash, pruritus, ankle edema, excessive perspiration, weight gain, nasal congestion. Some of the CNS and genitourinary symptoms may be related to the underlying disease rather than to drug therapy.
The following laboratory tests have been found to be abnormal in a few patients receiving Lioresal: increased SGOT, elevated alkaline phosphatase, and elevation of blood sugar.

OVERDOSAGE

Signs and Symptoms:
Vomiting, muscular hypotonia, drowsiness, accommodation disorders, coma, respiratory depression, and seizures.

Treatment:
In the alert patient, empty the stomach promptly by induced emesis followed by lavage. In the obtunded patient, secure the airway with a cuffed endotracheal tube before beginning lavage (do not induce emesis). Maintain adequate respiratory exchange, do not use respiratory stimulants.

DOSAGE AND ADMINISTRATION

The determination of optimal dosage requires individual titration. Start therapy at a low dosage and increase gradually until optimum effect is achieved (usually between 40-80 mg daily).
The following dosage titration schedule is suggested:
5 mg t.i.d. for 3 days
10 mg t.i.d. for 3 days
15 mg t.i.d. for 3 days
20 mg t.i.d. for 3 days
Thereafter additional increases may be necessary but the total daily dose should not exceed a maximum of 80 mg daily (20 mg q.i.d.).
The lowest dose compatible with an optimal response is recommended. If benefits are not evident after a reasonable trial period, patients should be slowly withdrawn from the drug (see WARNINGS *Abrupt Drug Withdrawal).*

HOW SUPPLIED

Tablets 10 mg – oval, white, scored (imprinted Lioresal on one side and 10 twice on the scored side)
Bottles of 100…….NDC 0028-0023-01
Unit Dose (blister pack)
Box of 100 (strips of 10)……NDC 0028-0023-61
Tablets 20 mg – capsule - shaped, white, scored (imprinted Lioresal on one side and 20 twice on the scored side)
Bottles of 100…….NDC 0028-0033-01
Unit Dose (blister pack)
Box of 100 (strips of 10)……NDC 0028-0033-61
Do not store above 30ºC (86ºF). Dispense in tight container (USP).
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Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936